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EXAMINER
SCHNIZER, RICHARD A

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 11/27/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

Offic Action Summary	Application No. 09/446,317	Applicant(s) WAGNER ET AL.	
	Examiner Richard Schnizer	Art Unit 1632	

-- The MAILING DATE of this communication appears on the cover sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

An amendment and the Declaration of Dr. Manfred Ogris were received an entered as Paper No. 17 on 8/28/01. Claim 53 was canceled as requested. Claims 35-52 and 54-68 remain pending and are under consideration in this Office Action.

Rejections Withdrawn

The rejection of claims 54-57 and 65-68 under 35 USC 112, first paragraph is withdrawn in view of Applicant's amendments.

The rejection of claims 58-63 under 35 USC 112, second paragraph is withdrawn in view of Applicant's amendments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 35-43, 49, and 65 are rejected under 35 U.S.C. 102(e) as being anticipated by either one of Yin (1995) or Tomalia (1995).

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column. 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28; column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are disclosed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5, lines 44-50; and claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. See column 18, lines 41-43; column 54, claim 41; and column 57, claim 63.

Thus Yin anticipates the claims.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10.

Thus Tomalia anticipates the claims.

Claims 35, 41-45, 49, 52, and 65 are rejected under 35 U.S.C. 102(e) as being anticipated by Bogdanov et al (1994).

Bogdanov teaches a drug delivery composition comprising PEI to which PEG has been covalently attached as a protectant. Polynucleotides may be present as a block copolymer with PEI. See column 5, lines 10-16, and 59-66. The composition may also comprise a targeting group bound to either PEI or PEG. See column 6, lines 36-40. PEG may be present in molecular weight from 500-10,000 D. See column 15, lines 47-50.

Thus Bogdanov anticipates the claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 35, 42, 44-51, 58-64, and 66 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yin et al (1995) or Tomalia et al (1995), either one in view of Szoka (1995).

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column. 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28;

column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are disclosed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5, lines 44-50; and claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. See column 18, lines 41-43; column 54, claim 41; and column 57, claim 63. The complex may be formed in water. See column 29, lines 35-39.

Yin is silent with respect to the molecular weight of the hydrophilic polymer, the ratio of hydrophilic polymer to PEI primary amine groups, and the order in which the DNA and the hydrophilic polymer are added to PEI. Yin does not teach transferrin or EGF as targeting ligands.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10. The complex may be formed in water. See column 49, lines 4-12.

Tomalia is silent with respect to the molecular weight of the hydrophilic polymer, the ratio of hydrophilic polymer to PEI primary amine groups, and the order in which the DNA and the hydrophilic polymer are added to PEI. Tomalia does not teach transferrin or EGF as targeting ligands.

Szoka teaches a self-assembling polynucleotide delivery system comprising dendrimer polycations. The dendrimers are composed of cationic polyamines similar to polyethylenimine. See column 10, lines 36-46. The complexes may comprise a DNA masking agent, such as PEG, covalently linked to the dendrimer. The PEG may have a molecular weight from 700-20,000 D, and may be present in a ratio of moles of polymer:PEI primary amino groups from 1:3 to 1:33. See column 12, lines 18-43. Szoka also encourages the use of EGF as a targeting ligand, and discloses that transferrin is well known in the art as a targeting ligand. See column 2, lines 43-45; column 3, lines 40-44; and column 14, lines 8-11.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use PEG in the inventions of either Yin or Tomalia in the molecular weights and ratios taught by Szoka. Yin and Tomalia are silent on the molecular weights and ratios of PEG to use in their compositions, but one of ordinary skill in the art would be aware of the teachings of Szoka, and would be motivated to use these molecular weights and ratios of PEG as a starting point in the optimization of the complexes because the compositions of Szoka are very similar in structure and function to those of Yin and Tomalia. For example, the compositions all comprise cationic polyamines with primary amino groups involved in a charge interaction with nucleic acid and a

hydrophilic polymer at the periphery of the polymer, and the intended use of the compositions is the delivery of nucleic acids to cells.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the PEI/DNA/PEG complexes of Yin and Tomalia by first mixing the DNA and PEI, and then adding the PEG. One would have been motivated to take this approach because Szoka teaches that PEG is useful as a masking agent which shields DNA from degradation. As such, it would be obvious to add it to the complex after addition of DNA, thereby maximizing the likelihood that the DNA would be masked. It would have been similarly obvious to use DNA concentrations of about 5-50 or 10-40 microgram/ml at a salt concentration below the physiological value in this process because Yin and Tomalia both teach the use of DNA at a concentration of 50 microgram/ml in water for the formation of complexes. The use of deionized water is standard operating procedure in molecular biology laboratories, as is well known by one of ordinary skill in the art. Further optimization of the concentration of the complexes for the purpose of transfection is well within the ability of one of ordinary skill in the art, and could reasonably be expected to lead to compositions with the characteristics of those of claims 63 and 64. The concentration of the complexes can be viewed as a result-effective variable which is routine in the art to optimize.

Thus the invention as a whole was prima facie obvious.

Claim 52 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Yin or Tomal.ia et al, either one in view of Szoka, as applied to claims 44-51, and 64 above, and further in view of Bogdanov et al. (US Patent 5,871,710, effective filing dale of 6/17/94) for the reasons of record in Paper Nos. 6 and 13.

The teachings of Szoka and either of Yin or Tomalia can be combined to disclose a complex comprising PEI, DNA, a hydrophilic polymer covalently bound to PEI, and a targeting ligand bound to PEI. These references do not teach a targeting ligand bound to the hydrophilic polymer which is bound to PEI

Bogdanov teaches a drug delivery composition coml)rising PEI to which PEG has been covalently attached as a protectant. See column 5, lines 10-16, and 59-60. The composition may also comprise a targeting group bound to either PEI or PEG. See column 6, lines 36-40.

It would have been obvious to one of ordinary skill in the art to attach the targeting ligand of Szoka and either Yin or Tomalia to the hydrophilic polymer rather than to PEI because Bogdanov suggests doing so. One would have been motivated to do this in order to expose the target.

Claims 35, 54, 65 and 67 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Yin (1995) or Tomalia (1995), in view of Mizushima et al (Nucl. Acid, Res. 18(17): 5322, 1990).

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column. 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28; column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are disclosed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5, lines 44-50; and claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. See column 18, lines 41-43; column 54, claim 41; and column 57, claim 63.

Yin does not teach a nucleic acid encoding a cytokine.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10.

Tomalia does not teach a nucleic acid encoding a cytokine.

Mizushima teaches a method of transfecting cells in vitro by incubating with DEAE-dextran a nucleic acid encoding the cytokine human G-CSF. See abstract.

It would have been obvious to one of ordinary skill in the art to substitute the PEI/DNA transfection complexes for the DEAE-dextran method of Mizushima. One would have been motivated to do so because Yin teaches that PEI DNA complexes give high transfection efficiency in the absence of DEAE dextran, and that DEAE dextran is cytotoxic. See column 31, lines 44-51. Furthermore, Tomalia teaches that transfection results obtained using PEI/DNA transfection complexes are superior to those obtained using DEAE-dextran. See sentence bridging columns 54 and 55.

Thus the invention as a whole was *prima facie* obvious.

Claims 35, 65, and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Tomalia (1995) or Yin (1995), in view of Sompayrac et al (Proc. Nat. Acad. Sci. USA 78(12): 7575-7578, 12/1981).

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column. 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28; column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are disclosed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5, lines 44-50; and claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. See

column 18, lines 41-43; column 54, claim 41; and column 57, claim 63.

Yin does not teach a nucleic acid encoding a tumor antigen.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10.

Tomalia does not teach a nucleic acid encoding a tumor antigen

Sompayrac teaches a method of transfecting cells in vitro by incubating with DEAE-dextran a nucleic acid encoding SV-40 tumor antigen. See abstract.

It would have been obvious to one of ordinary skill in the art to substitute the PEI/DNA transfection complexes for the DEAE-dextran method of . One would have been motivated to do so because Yin teaches that PEI DNA complexes give high transfection efficiency in the absence of DEAE dextran, and that DEAE dextran is cytotoxic. See column 31, lines 44-51. Furthermore, Tomalia teaches that transfection results obtained using PEI/DNA transfection complexes are superior to those obtained using DEAE-dextran. See sentence bridging columns 54 and 55.

Thus the invention as a whole was *prima facie* obvious.

Claims 35, 56 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over either one of Tomalia (1995) or Yin (1995), in view of Obaru et al (Human Gene Therapy 7(18): 2203-2208, 1996).

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column. 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28; column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are disclosed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5, lines 44-50; and claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. See column 18, lines 41-43; column 54, claim 41; and column 57, claim 63.

Yin does not teach a nucleic acid encoding herpes simplex thymidine kinase.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10.

Tomalia does not teach a nucleic acid encoding herpes simplex thymidine kinase.

Obaru teaches a method of transfecting cells in vitro by incubating with DEAE-dextran a nucleic acid encoding herpes simplex thymidine kinase. See abstract.

It would have been obvious to one of ordinary skill in the art to substitute the PEI/DNA transfection complexes for the DEAE-dextran method of Obaru. One would have been motivated to do so because Yin teaches that PEI DNA complexes give high transfection efficiency in the absence of DEAE dextran, and that DEAE dextran is cytotoxic. See column 31, lines 44-51. Furthermore, Tomalia teaches that transfection results obtained using PEI/DNA transfection complexes are superior to those obtained using DEAE-dextran. See sentence bridging columns 54 and 55.

Thus the invention as a whole was *prima facie* obvious.

Response to Arguments

Applicant's arguments, and the Declaration of Dr. Ogris, filed 8/25/01 have been fully considered but they are not persuasive.

Applicant argues at pages 6 and 7 of the response that "PEI" is an art recognized term, and that the PEI of the invention is limited to the PEI disclosed in the specification, rather than the PEI disclosed in the prior art cited by the PTO. Applicant relies for support on the Declaration of Dr. Ogris. The Declarant provides several examples (Exhibits 1-4) which describe various forms of PEI. The Declarant states that PEI may take several forms including

random short branched, random long branched, regular comb branched, and regular star branched polymers, and that one of ordinary skill in the art would recognize the term "PEI", when used alone and without any modifying adjective to mean random branched chain PEI, and not one of the more unusual forms of PEI such as linear PEI, dendritic PEI, or hyper comb branched PEI.

The position of the PTO is that "PEI" is a generic term encompassing all types of polyethyleneimine polymers including linear, random short branched, random long branched, regular comb branched, regular star branched, dendritic, and hyper comb branched. It is apparent from the art of record that when those of skill in the art wish to make clear that they are working with a specific type of PEI, they take care to point out the particular characteristics of the molecule. For example, Coll (Exhibit 2), who "analyzed the potential of a synthetic polymer, polyethyleneimine (PEI) (Boussiff et al. 1995), to achieve efficient gene transfer into tumor cells" (see page 1660, third full paragraph), was careful to refer to the particular version of PEI used, "linear PEI", in the title of the article. The assertion that one of ordinary skill in the art would recognize PEI as meaning "random branched chain" polyethyleneimine lacks support and is contradicted by the Exhibits 3 and 4. Godbey (Exhibit 3) defines PEI as the generic "poly(ethyleneimine)", and as a polymer which "comes in two forms, linear and branched." See first sentence of abstract, and page 150, column 1, lines 1-4. In contrast, Klotz (Exhibit 4) requires that PEI must be branched, defining it as a "highly branched water soluble molecule". See page 4753, column 1, lines 5 and 6. Thus there is no consensus that "PEI", in the absence of

any modifier means "random branched chain PEI". In any case, it is not clear how the broad definition of Klotz would exclude any of the branched forms of PEI disclosed by Yin or Tomalia.

With regard to the assertion that the PEI of the invention is limited to the PEI disclosed in the specification, it is noted that neither the claims nor the specification place limits on the type of PEI which may be used in the invention. Thus this assertion is unsupported.

Applicant argues at page 9 of the response that Tomalia does not teach covalent attachment of hydrophilic polymers to the PEI polymer. Applicant's attention is directed to column 30, lines 25-31 which states that PEG may be "attached to the dendrimer surface". Applicant admits that "attachment" encompasses covalent linkage, but argues that because this definition was given in the context of "carried materials" physically entrapped or encapsulated within the core of dendrimers, it does not apply to PEG because PEG is not defined as a "carried material" and is present on the surface of the dendrimer. Applicant's attention is directed to column 53, lines 1-45 which describes the chemical reactions by which biotin and pyruvate are attached to the surface of a dendrimer. Clearly the mechanism of attachment is covalent, thus the term "attachment" also refers to covalent linkage in the context of the surface of the dendrimer. Because PEG may be attached to the surface of the dendrimer, it would have been obvious to one of ordinary skill in the art obvious that such attachment could be by covalent means.

Applicant argues at page 10 of the response that Bogdanov fails to teach PEI/nucleic acid complexes. The issue is the definition of the term "complex". Applicant argues that it is clear from the claims, the teachings of the art, and the specification that the claimed complex between

PEI and DNA is an electrostatic association. For support, Applicant relies on Exhibits C-E. Exhibit C is a definition from the Merriam Webster Collegiate Dictionary indicating that a complex is an association between two or more species "joined usually by weak electrostatic bonds rather than covalent bonds." The PTO notes that this definition does not exclude covalent bonds from complexes. Exhibit D is a definition of complex within the context of metal ions. Exhibit E is an example of ionic PEI/DNA complexes. Neither of these Exhibits provides support for the position that a complex must be ionic, rather than covalent. It is the position of the PTO that the term "complex" is a generic term which encompasses both ionic and covalent complexes. Clearly, "covalent complex" is a term of art, as a Medline search of the term "a covalent complex of" returned 156 hits. Items 150-156 of this search are enclosed as a courtesy to Applicant. Neither the claims nor the specification excludes covalent complexes from the scope of the invention, therefore Bogdanov anticipates the claims.

Applicant's arguments against the rejections under 35 USC 103 are based upon the alleged deficiencies of Yin, Tomalia, and Bogdanov, and depend upon the definitions of "PEI", "attachment", and "complex". These issues have been completely addressed above.

For these reasons the rejections are maintained.

Conclusion

No claim is allowed.

Due to a typographical error in the previous Office Action, claims 58-62 were inadvertently omitted from the obviousness rejection over Tomalia or Yin in view of Szoka. The 103 rejections have also been corrected to include parent claims which were previously omitted. For these reasons, the rejections are non-final.

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Patsy Zimmerman whose telephone number is 703-308-8338.

Richard Schnizer, Ph.D.

JAMES KETTER
PRIMARY EXAMINER